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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SHARAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 06/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/293,835	KENNEDY ET AL.	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,15,19,24,28-39,41-47 and 49-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☒ Claim(s) *1,15,19,24,28-39,41-47 and 49-55* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 14, 2005 has been entered.

Claims 1, 15, 19, 24, 28-39, 41-47, 49-55 are pending. Any rejection that is not addressed in this Office Action is considered moot in view of new grounds of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 52-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 52 recites the limitation "said disorder" in line 5. There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 15, 19, 24, 28-39, 41-47, 49-55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating

onychomycosis with 5-aminolevulinic acid (5-ALA), does not reasonably provide enablement for methods of treating all fungal diseases including onychomycosis with any agent which is not in itself a photosenitizer but which induces accumulation of protoporphyrin IX in a cellular target. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. However, these factors are illustrative, not mandatory and what is relevant depends on the specific facts. All of these factors need not be reviewed when determining whether a disclosure is enabling. *Id.* When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The invention provides for methods of treating any fungal infection at any site within a patient body with any agent which is not in itself a photosensitizer but which induces accumulation of protoporphyrin IX in a cellular target by photoactivating the protoporphyrin IX.

(2) The state of the prior art

The state of art is directed to methods of phtodynamically treating infections with 5-ALA, benzoprotoporphyrins or derivatives thereof.

(3) The relative skill of those in the art

The relative skill of the those in the art is high and encompass anyone with understanding of clinical radiology.

(4) The predictability or unpredictability of the art

The unpredictability of the clinical medicine is very high. The art at the time of invention was essentially directed to methods of administering photodynamic therapy by administering effective amounts of a photosensitizing agent. Aside from 5-ALA, the use of agents that are not photosensitizer, but induce accumulation of protoporphyrin IX in a cellular target was not well described. In fact, there is no predictability that

protoporphyrins IX synthesis is induced in the target cells. Accordingly, there is not predictability in the art and apprasing the entire scope of the instant claims requires pain staking experimental study.

(5) The breadth of the claims

The claims are very broad. The claims are directed to methods of treating any fungal infection by administering an agent which is not in itself a photosensitizer but which induces accumulation of protoporphyrin IX in a cellular target. The scope of applicable agents that can provide the claimed function is unknown. Further, their utility in treating all types of fungal infections, their reach to deep layered tissues, etc.. are not described.

Further, the instant claims appear to place a function at the point of novelty of the instant methodology. Attention is directed to *General Electric Company v. Wabash Appliance Corporation et al* 37 USPQ 466 (US 1938), at 469, speaking to functional language at the point of novelty as herein employed: "the vice of a functional claim exists not only when a claims is "wholly" functional, if that is ever true, but when the inventor is painstaking when he recites what has already been seen, and then uses conveniently functional language at the exact point of novelty". Functional language at the point of novelty, as herein employed by Applicants, is further admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC 1997) at 1406: stating this usage does "little more than outlin[e] goals appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate".

As it has repeatedly been stressed by the Courts, an assay for determining whether a given compound possesses certain desired characteristics and identifies some broad categories of compound that might work, these descriptions, without more precise guidelines, amount to little more that "a starting point, a direction for further research." See *Genetech v. Novo Nordisk A/S,* 108 F.3d 1361,1366,(Fed. Cir.), also *Enzo Biochem, Inc. V. Calgene*, Inc, 1888 F.3d 1362, 1374 (Fed. Cir. 1999).

Here, Applicants functional language at the point of novelty fails to meet the requirements set forth under 35 USC 112, first paragraph, because it does not with reasonable degree of certaintly elaborate on the scope of the instant claims. Claims employing functional language at the point of novelty, such as Applicants', neither provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limits of the monopoly asserted"

(6) The amount of direction or guidance presented

The instant claims merely calls for the use of a trial and error to attempt to find a agents that will improve treatment of fungal infections. The instant specification first fails to identify potential useful agents or their mechanism of action for screening. Even though the specification may provide for an exemplary drug from the group of such compounds as 5-ALA, it does not provide necessary link between finding a particular compound or narrowing the range of candidates in order to find a suitable compound without the need for undue experimentation. Given the broad breadth of the claims the

ordinary skill in the art would not have any guidance as what type of compounds should he proceed with.

(7) The presence or absence of working examples

The specification merely provides examples directed to the use of 5-ALA. There are no other types of compounds described for the intended benefits. In fact, there is no evidence provided in the specification showing that all possible nonphotosensitzers do in fact cause accumulation of protopohyrin IX in the cellular target of interest.

(8) The quantity of experimentation necessary

Since the significance of agents which are not in itself a photosenistzer, but which induced accumulation of protoporphyring IX in a cellular target and their biological activity cannot be predicted a priori but must be determined from the case to case by painstaking experimental study and when the above factors are weighed together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine the all of the possible disease states or all the agents suitable for the intended benefits. Thus, practicing the entire scope of the instant claims require undue experimentation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1, 15, 19, 24, 28-39, 41-47, 49-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levy et al US Patent 5,283,255 in view of Richter et al US Patent 5,705,518.

Levy teaches methods of treating infections comprising topically administering to a patient benzoporphyrins which are derivatives of protoporphyrin-IX. (see abstract) Levy further administers light to the site of interest where benzoporphyrin is applied. (see abstract, col 7, lines 3-35). Levy states that photodynamic treatment is effective for treating athlete's foot. Specifically, Levy indicates that his methodology can be employed for treating fungal infections (see col 19, line 4, and lines 19-24). It is established in the art that athlete's foot is caused by tinea pedis and leads to similar pathophysiological conditions as onychomycosis. Levy does not teach the use of 5-aminolevulinic acid as a photoactive agent for his methodology.

Richter teaches that photosensitive compounds include prodrugs such as 5-aminolevulinic acid which can produce drugs such as protoporphryin (see col, lines 59-65; col 5, lines 61-67). The prodrug of Richter provides the same effect in vivo as other photosensitizing agents such as porphyrins and benzoporphyrins.(col 5, lines 61-col 6, line 5). In fact, Richter characterizes 5-aminolevulinic acid to functionally provide the same effects as benzoporphyrins. Richter teaches topical administration of the prodrug prior to employing photodynamic therapy (col 6, lines 8-20). Richter does not teach treatment of fungal skin conditions.

However, it would have been obvious to one of ordinary skill in the art at the time of invention to employ 5-aminolevulinic acid, taught by Richter, in methodology of Levy,

because as taught by Richter, other functional equivalents such as aminolevulinic acid is expected to produce the same effects as protoporphyrin and benzoporphyrins. Since Levy teaches effectiveness of benzoporphyrins in treating skin infections caused by *tinea pedius*, the ordinary skill in the art would have had a reasonable expectation of success to achieve the same results when employing 5-aminolevulinic acid of Richter.

Response to Arguments

4. Applicant's arguments filed on January 14, 2005 have been considered but are not persuasive.

Applicant first argues that Levy's teachings is not for treating onychomycosis and that the understanding of the art at the time of invention would not have directed one of skilled in the art to use photodynamic therapy for treating onychomycosis (see Arguments at page 7-8).

In response Examiner states that only 50, 52-55 are directed to methods of treating onychomycosis. Therefore, Applicant's arguments at least with respect to claims 1, 15, 19, 24, 28-39, 41-47, 49, 51 are not commensurate with the scope of the claims because none of such claims are directed to methods of treating onychomycosis in a patient in need thereof.

With respect to claims 50, 52-55, Examiner states that the instant claims do not comprise any manipulatively different step from those of the cited art. All that is required in the pending claims is to administer an agent and exposing the patient to light capable of photoactiviating protoprphyrin IX.

Further, for the purposes of clarifying the claim interpretation, Examiner views that some of the recited limitations in the pending claims are not positively limiting the pending claims. For example, the language of "light capable of photoactivating protoporphyrin IX" in claims 1, 19, 36, and 44 are not a positive limitation, because protoporphyrin IX is an endogenous photosensitizer and inherently made in the body at the presence of any source of light. Thus, exposing a patient to a light capable of photoactivating protoporphryin IX does not positively limit the claims, because since protoporphyrin IX is endogenously made in the body, the instant claim language encompass any source of light that a patient is exposed to.

Moreover, the limitation of "the presence of the lesions or cellular abnormalities in the nail" in claims 50, 52-55 is also not a positive element. Note that the instant claims are directed to methods of treating onychomycosis wherein the onychomycosis is characterized by the presence of lesion or cellular abnormalities of the nail. Examiner does not recognize the limitation "said disorder is characterized by the presence of lesion or cellular abnormalities of the nail" to limit the conditions or symptoms of onychomycosis, because such characterization is already encompassed in the term onychomycosis. Simpley, onychomycosis is a fungal infection of nail characterized by lesions and cellular abnormalities.

Therefore, the scope of the pending claims pending claims are essentially directed to methods of treating a fungal infection by administering an agent to a patient and then exposing the patient to any radiation capable of inducing the synthesis of protoporphyrin IX. The steps described by Levy and Richter disclose a photodynamic

method comprising administering a photodynamic agent and exposing the patient to light capable of photoactivating protoprophyrin IX. Richter simply establishes that one of ordinary skill in the art would have had the understanding that benzoporphyrins of Levy and 5-ALA of Richter are art recognized functional equivalents and thus interchangeable when used for the same purpose.

[F]or obviousness under §103, all that is required is a reasonable expectation of success. *In re Longi*, 759 F.2d 887, 897, 225 USPQ 645, 651-52 (Fed. Cir. 1985). Obviousness does not require absolute predictability of success. As has previously reasoned, Levy teaches that fungal infection can be treated with benzoporphyrins and employing photodynamic therapy. Richter further states that 5-aminolevulinic acid is a suitable photosensitizing agent as benzoporphyrins of Levy. Thus, the combined teachings of Levy and Richter provides reasonable expectation of success to one of ordinary skill in the art to use 5-aminolevulinic acid in place of benzoporphyrins of Levy in treating a fungal infection.

Conclusion

5. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The

fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SREENI PADMANABHAN
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